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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/778,187	02/06/2001	Peter Robert Baum	2873-US	9057

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EXAMINER
ROARK, JESSICA H

ART UNIT	PAPER NUMBER
1644	17

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Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/778,187	Applicant(s) BAUM ET AL.	
	Examiner Jessica H. Roark	Art Unit 1644	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *08 November 2002* .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *18-63* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *18-63* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☒ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☒ Information Disclosure Statement(s) (PTO-1449) Paper No(s) *2, 14* .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Applicant's amendment, filed 11/8/02 (Paper No. 13), is acknowledged.
Claims 1-17 have been canceled.
Claims 18-63 have been added and *are pending.*

2. Applicant's election without traverse of Group II with a species election of the human polypeptide in Paper No. 13 is acknowledged.

After further consideration and in view of the extensive sequence identity shared between the human and mouse polypeptides, the species requirement is withdrawn. The instant claims have been searched with respect to both SEQ ID NO:2 and SEQ ID NO:4.

Claims 18-63 *are under consideration in the instant application.*

3. It is noted that the specification on page 10 at lines 8-13 discloses that a polypeptide encoded by a nucleic acid that is "degenerate, as a result of the genetic code" compared to a reference nucleic acid does not differ in amino acid sequence compared to the polypeptide encoded by the reference nucleic acid.

Claim Rejections - 35 USC § 112 second paragraph

4. The following is a quotation of the second paragraph of 35 U.S.C. 112.
The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

5. Claims 18-63 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A) Claims 18-63 are indefinite in that they only describe the "LDCAM polypeptide" and "B7-L1 polypeptide" to which the claimed polypeptide binds by arbitrary protein names. There is nothing in the claims which establishes the metes and bounds of which polypeptides can be considered a "LDCAM polypeptide" or "B7-L1 polypeptide". Consequently, the metes and bounds of the polypeptide which binds are not established.

It is suggested that Applicant amend the claims to include a recitation of a SEQ ID NO(s) for each of the "LDCAM" and "B7-L1" polypeptides to either of which the instantly claimed polypeptides must bind.

B) Claims 35, 36 and 46-54 are ambiguous in reciting hybridizing under conditions of "moderate stringency" (claims 35 and 46-54) or "severe stringency" (claim 36). There does not appear to be a definition in the specification as filed that clearly provides the metes and bounds of these conditions. Thus it is unclear which conditions are actually claimed.

C) Applicant is reminded that any amendment must point to a basis in the specification so as not to add new matter. See MPEP 714.02 and 2163.06.

Claim Rejections - 35 USC § 112 first paragraph

6. The following is a quotation of the first paragraph of 35 U.S.C. 112:

The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

7. Claims 18-63 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for:

SEQ ID NOS:2 and 4 (encoded by the DNAs of SEQ ID NOS:1 and 3); internal fragments of SEQ ID NO:2 or 4; polypeptides *comprising* fragments of SEQ ID NO:2 or 4 wherein the fragment is the extracellular domain of SEQ ID NO:2 or 4 and the polypeptide binds the "LDCAM" polypeptide of SEQ ID NOS:2 or 4 or binds the "B7-L1" polypeptide of SEQ ID NOS:8 or 10; and polypeptides *of limited sequence variation* that bind the "LDCAM" polypeptide of SEQ ID NOS: 2 or 4 or bind the "B7-L1" polypeptide of SEQ ID NOS: 8 or 10;

does not reasonably provide enablement for polypeptides that

a) comprise a sequence that has "at least 80% (or 90%) identical" (e.g., claims 18-21);

b) binds to any "LDCAM" or "B7-L1" polypeptide (all pending claims);

c) *comprises* fragments other than the extracellular domain (e.g., claims 22-34); or

d) comprise an amino acid sequence "variance" of unlimited number of insertions, deletions, or substitution (e.g., claims 55-63).

The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the invention commensurate in scope with these claims.

A) and D) "Variant Polypeptides":

The state of the art at the time the invention was made recognized that it was unpredictable if any functional activity will be shared by two polypeptides having less than 100% identity over the full length of their sequences. Attwood (Science 2000; 290:471-473) teaches that "[i]t is presumptuous to make functional assignments merely on the basis of some degree of similarity between sequences. Similarly, Skolnick et al. (Trends in Biotech. 2000; 18(1):34-39) teach that the skilled artisan is well aware that assigning functional activities for any particular protein or protein family based upon sequence homology is inaccurate, in part because of the multifunctional nature of proteins (e.g., "Abstract" and "Sequence-based approaches to function prediction", page 34). Even in situations where there is some confidence of a similar overall structure between two proteins, only experimental research can confirm the artisan's best guess as to the function of the structurally related protein (see in particular "Abstract" and Box 2). Finally, even single amino acid differences can result in drastically altered functions between two proteins. For example, Metzler et al. (Nature Structural Biol. 1997; 4:527-531) show that any of a variety of single amino acid changes can alter or abolish the ability of CTLA4 to interact with its ligands CD80 and CD86 (e.g., summarized in Table 2).

The scope of the instant claims reciting polypeptides that (A) comprise a sequence that has "at least 80% (or 90%) identity" or (D) comprise an amino acid sequence "variance" of unlimited number of insertions, deletions, or substitution encompasses a great deal of variation in the polypeptide sequence. A polypeptide that comprises an amino acid sequence "variance" of unlimited number of insertions, deletions, or substitution is essentially any sequence since the number of changes that can be made to the sequence is unlimited. Given the extensive variation permitted by the instant claim language, the skilled artisan would not reasonably expect such "variant" polypeptides to have the same function as the instantly recited SEQ ID NOS.

The specification does not appear to provide sufficient guidance as to which residues should or should not be changed to preserve the recited function of binding either a LDCAM or B7-L1 polypeptide. Although the specification does provide working examples of human and mouse LDCAM polypeptides of SEQ ID NOS:2 and 4, the variation permitted by the instant claim language is extensive. Consequently, the experimentation left to those skilled in the art to determine which "variant" sequences would still result in polypeptides having the same function as a the human and mouse LDCAM polypeptides disclosed in the specification as filed is unnecessarily, and improperly, extensive and undue.

It is suggested that Applicant limit the claims to variant nucleic acids sequences having only limited variation (e.g. 95% identity) over the full length of the sequence, AND possessing testable functional activity supported in the specification and priority documents (e.g., binding a particular "LDCAM" or "B7-L1" polypeptide, as provided by inclusion of a SEQ ID NO:).

B) A Polypeptide that binds *any* "LDCAM" or B7-L1" Polypeptide:

The skilled artisan lacks sufficient guidance with respect to the scope of polypeptides which bind to *any* "LDCAM" or *any* "B7-L1" polypeptide. As noted supra, the terms "LDCAM" and "B7-L1" are ambiguous as currently recited. Neither the skilled artisan nor the state of the art at the time the invention was made recognized either a "LDCAM" or "B7-L1" polypeptide as an art-recognized group of molecules.

The scope of the instant claims encompass a polypeptide that binds to any "LDCAM" or "B7-L1" polypeptide. In the absence of sufficient structural information (e.g., amino acid sequence, etc.), there is insufficient guidance and direction to allow the skilled artisan to determine whether any particular polypeptide is either a "LDCAM" or "B7-L1" polypeptide without the need for further undue experimentation. The instant claims are essentially a "wish to know" the identity of any polypeptide which can be construed to be a "LDCAM" or a "B7-L1" polypeptide. It has been previously decided that claims recitations so broad do not provide sufficient guidance as to how to make and use the claimed invention. See Colbert v. Lofdahl, 21 USPQ2d, 1068, 1071 (BPAI 1992). Since insufficient guidance appears to have been provided regarding the polypeptide(s) to which the instantly recited polypeptide binds; undue experimentation would be required to make and use the instantly recited polypeptides that bind.

C) "Fragments *Comprising*":

The instant claims recite in various forms polypeptides comprising "fragments" of a certain number of amino acid residues of the various SEQ ID NOS (or encoding nucleic acids). "Comprising" language opens the claim up to the inclusion of additional residues of undisclosed identity and number flanking the recited "fragment". The skilled artisan can make fragments *limited* to *sub*sequences of the individual SEQ ID NOS without undue experimentation. However, before the skilled artisan can make polypeptides comprising "fragments" with additional flanking sequence, guidance is required with respect to the identity of those flanking sequences. In the instant case however, the specification does not appear to provided this needed guidance. Therefore the scope of the instant claims encompassing "fragments comprising" does not appear to be commensurate with the enablement provided by the instant disclosure. In addition, it is unpredictable if a fragment other than a fragment that is the extracellular domain would have the instantly recited function of binding a LDCAM or B7-L1 polypeptide (even were the LDCAM and B7-L1 polypeptides defined by SEQ ID NOS). The specification does not appear to provide guidance as to which fragments other than the fragments comprising the extracellular domain would have this activity. Therefore the scope of the instant claims does not appear to be commensurate with the enablement provided by the instant disclosure.

Reasonable correlation must exist between the scope of the claims and scope of enablement set forth. For the reasons set forth supra, the experimentation left to those skilled in the art with respect to the instantly recited limitations is unnecessarily, and improperly, extensive and undue.

Claim Rejections – 35 U.S.C. §§ 102 and 103

8. The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

A person shall be entitled to a patent unless --

(e) the invention was described in (1) an application for patent, published under section 122(b), by another filed in the United States before the invention by the applicant for patent or (2) a patent granted on an application for patent by another filed in the United States before the invention by the applicant for patent, except that an international application filed under the treaty defined in section 351(a) shall have the effects for purposes of this subsection of an application filed in the United States only if the international application designated the United States and was published under Article 21(2) of such treaty in the English language.

9. Claims 18-63 are rejected under 35 U.S.C. 102(e) as being anticipated by Baker et al. (US 2002/0198147), as evidenced by the attached alignments.

Baker et al. teach the isolated PRO355 polypeptide set forth in SEQ ID NO:61.

The PRO355 polypeptide is 100% identical to the instant polypeptide of SEQ ID NO:2 from position 39 to position 442. PRO355 differs from the instant polypeptide of SEQ ID NO:2 only by an internal deletion of two amino acid residues in the signal sequence corresponding to positions 24 and 25 of instant SEQ ID NO:2.

PRO355 therefore also is a polypeptide 100% identical to the instant polypeptide of SEQ ID NO:4 from position 8 to position 423. PRO355 differs from the instant polypeptide of SEQ ID NO:4 by an internal deletion of two amino acids in the signal sequence corresponding to positions 6 and 7 of instant SEQ ID NO:2 and by an additional amino acid at the C terminus.

Baker et al. also teach the nucleic acid of SEQ ID NO:60 which encodes the PRO355 polypeptide of SEQ ID NO:61. The nucleic acid of SEQ ID NO:60 would hybridize to the complement of SEQ ID NO:1, including from 16 or 130 to 1137; and would hybridize to the complement of SEQ ID NO:3, including from 1 or 62 to 1069, under moderate or severe stringency in view of the sequence identity between the nucleic acid of SEQ ID NO:60 of Baker et al. and the instant SEQ ID NOS:1 and 3 encoding SEQ ID NOS:2 and 4.

Baker et al. also teach methods of producing the PRO355 polypeptide by culturing a host cell transfected with the nucleic acid of SEQ ID NO:60 (see e.g., paragraph 297).

Baker et al. also teach fusion polypeptides comprising the PRO355 polypeptide or a soluble extracellular domain (i.e., a fragment) thereof, including a fusion polypeptide comprising an Fc region (e.g., paragraphs 293-295).

Variants of the PRO355 polypeptide are also taught by Baker et al. (see e.g., paragraphs 180-187).

Compositions comprising the PRO355 polypeptide, fragments and variants thereof are taught at paragraphs 350-352.

The PRO355 polypeptide of Baker et al. inherently shares the functional properties of the instant polypeptides, including binding to a LDCAM polypeptide or a B7-L1 polypeptide. In addition, the PRO355 polypeptide would inherently form oligomers, including dimers, trimers or tetramers.

Applicant is reminded that no more of the reference is required than that it sets forth the substance of the invention. The claimed functional limitations would be inherent properties of the PRO355 polypeptide of Baker et al.

The reference teachings thus anticipate the instant claimed invention.

Conclusion

10. No claim is allowed.

11. Any inquiry concerning this communication or earlier communications from the examiner should be directed to Jessica Roark, whose telephone number is (703) 605-1209. The examiner can normally be reached Monday to Friday from 8:00 to 4:30. A message may be left on the examiner's voice mail service. If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, Christina Chan can be reached at (703) 308-3973. Any inquiry of a general nature or relating to the status of this application should be directed to the Technology Center 1600 receptionist whose telephone number is (703) 308-0196.

Papers related to this application may be submitted to Technology Center 1600 by facsimile transmission. Papers should be faxed to Technology Center 1600 via the PTO Fax Center located in Crystal Mall 1. The faxing of papers must conform with the notice published in the Official Gazette, 1096 OG 30 (November 15, 1989). The CM1 Fax Center telephone number is (703) 305-3014.

Jessica Roark, Ph.D.
Patent Examiner
Technology Center 1600
January 17, 2003

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